Proceedings – 23rd Annual Conference – IEEE/EMBS Oct.25-28, 2001, Istanbul, TURKEY

PRELIMINARY STUDY ON THE OXYGEN CONSUMPTION DYNAMICS DURING BRAIN HYPOTHERMIA RESUSCITION

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Abstract-**Based on the classical Pennes bioheat equation and oxygen diffusion equation, a new coupled heat-mass transfer model for characterizing the cerebral circulatory arrest is proposed. Two cooling approaches (the surface cooling and volumetric cooling) are applied to analyze the effect of hypothermia on the transient temperature and the oxygen consumption rate in different regions of brain. It is shown that the surface cooling contributes little to depress the oxygen consumption, which received few attentions before. As an alternative, the volumetric cooling will significantly reduce the oxygen consumption rate in the brain, thus prolong the patients' survival time. The results, which are close in agreement with the previous experimental data, may aid to find more efficient treatments on the brain hypothermia resuscitation.**

Keywords **- Circulatory arrest, hypothermia, brain cooling, oxygen consumption, resuscitation, hypoxia.**

I. INTRODUCTION

The brain is an organ whose normal function depends heavily on an uninterrupted delivery of oxygen. Unlike skeletal muscle that can survive for hours without oxygen, brain cells show irreversible damage within minutes from the onset of oxygen deficiency. When cardiopulmonary circulation is interrupted in many cardiac surgical procedures or accidental events, it will create an imbalance between energy production and consumption and cause rapid loss of oxygen and depletion of metabolic substrate. Under this adverse condition, the cerebral protection by hypothermia has been well established and commonly used clinically due to the decreased metabolic requirements of the cold brain tissues. There were extensive discussion on the effect of hypothermia and circulatory arrest on cerebral blood flow and metabolism [1]-[3]. Previous studies have found that total circulatory arrest allows patients survive for 60 minutes or more at 15-18^{o}C without any subsequent cerebral dysfunction and hypothermia is effective for protection against both global and focal brain ischemia. Reported experiments [4] suggested that the brain continues to metabolize at a very low basal rate during deep hypothermic circulatory arrest. But to our knowledge, few models have been developed to quantitatively investigate the effects of cerebral temperature changes during circulatory arrest to the oxygen consumption and how long could the patients withstand the oxygen delivery deficiency until all adenosine triphosphate (ATP) stored are depleted. Therefore, it is necessary to develop a mathematical model to address these issues and explore a better cooling approach to improve the patient's ability to survive in the hypoxia.

In this paper, based on the classical Pennes bioheat equation and oxygen diffusion equation, a new coupled heat-mass transfer model for characterizing the cerebral circulatory arrest is proposed. Two cooling approaches (the surface and volumetric cooling) are used to analyze the effect of hypothermia to the transient temperature and the oxygen consumption rate in different regions of the brain.

Ⅱ. METHODOLOGY

The present heat-mass coupling model falls in the appropriate assumption that the brain tissue can be approximately treated as a uniform sphere. The heat transfer can be represented by a one-dimensional Pennes bioheat equation in which the local brain temperature $T(r,t)$ is determined by

$$\rho C\frac{\partial T}{\partial t}=K\cdot\frac{1}{r}\frac{\partial^2(rT)}{\partial r^2}+W_b(T,Q_m)C_b(T_{\mathrm{a}}-T)+Q_m(t,T) \quad (1)$$

where ρ , C , K are density, specific heat and thermal conductivity of brain, respectively; C_b is specific heat of blood. These four thermal properties are treated as uniforrm and independent of temperature. Q_m is the metabolic heat generation rate; W_b is blood perfusion which may depends on local temperature and heat generation rate; T_a is the arterial temperature.

At steady state (normal condition), the one dimensional heat transfer problem can be established as:

$$K\cdot\frac{1}{r}\frac{\partial^2(rT)}{\partial r^2}+W_bC_b(T_a-T)+Q_{m0}=0 \quad (2)$$

with boundary conditions defined as:

$$-K\cdot\frac{\partial T}{\partial r}\Big|_{r=R_0}=h_{\mathrm{f}0}(T-T_{\mathrm{f}0})\,,\ r=R_0 \quad (3)$$

$$\frac{\partial T}{\partial r}=0\,,\ r=0 \quad (4)$$

where $h_{\mathrm{f}0}$ is the heat convention coefficient; $T_{\mathrm{f}0}$, R_0 denote the surrounding air temperature and radius of the brain hemisphere, respectively.

When cerebral circulation arrests, a transient state, the blood perfusion rapidly reduces to zero in short time, but the brain metabolism still keeps working until it runs out of

Report Documentation Page

Report Date	Report Type	Dates Covered (from... to)
25 Oct 2001	N/A	-

Title and Subtitle Preliminary Study on the Oxygen Consumption Dynamics During Brain Hypothermia Resuscition	**Contract Number**
	Grant Number
	Program Element Number
Author(s)	**Project Number**
	Task Number
	Work Unit Number
Performing Organization Name(s) and Address(es) Cryogenic Laboratory P.O. Box 2711 Technical Institute of Physics and Chemistry Chinese Academy of Sciences beijing 100080 P.R. China	**Performing Organization Report Number**
Sponsoring/Monitoring Agency Name(s) and Address(es) US Army Research, Development & Standardization Group (UK) PSC 802 Box 15 FPO AE 09499-1500	**Sponsor/Monitor's Acronym(s)**
	Sponsor/Monitor's Report Number(s)

Distribution/Availability Statement
Approved for public release, distribution unlimited

Supplementary Notes
Papers from 23rd Annual International Conference of the IEEE Engineering in Medicine and Biology Society, October 25-28, 2001, held in Istanbul, Turkey. See also ADM001351 for entire conference on cd-rom., The original document contains color images.

Abstract

Subject Terms

Report Classification unclassified	**Classification of this page** unclassified
Classification of Abstract unclassified	**Limitation of Abstract** UU

Number of Pages
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the metabolic substrate. Therefore, the transient brain temperature $T(r,t)$ can be described by the following heat transfer equation:

$$\rho C\frac{\partial T}{\partial t}=K\cdot\frac{1}{r}\frac{\partial^2(rT)}{\partial r^2}+Q_m(t,T) \qquad (6)$$

with the same boundary conditions as given above in the steady state. The initial condition is expressed as:

$$T(r,0)=T(r),\ t=0 \qquad (7)$$

Solving (6) satisfying the boundary and initial conditions yields the transient temperature distribution in the brain tissue.

But the toughest task is to evaluate the metabolic heat generation, which depends on the local brain temperature and time. To better deal with this problem, we aimed at developing a new metabolic heat generation model in this paper. The most widely used approach in estimating the metabolic term has been to set it to be the product of the oxygen consumption and its caloric value. But this is based on the assumption that oxygen, and not glucose, determines heat generation in tissues, which is improper for ischemic situation. During circulatory arrest, the metabolic rate decreases with that of the local temperature. It is assumed that the metabolic rate changes according to the temperature coefficient ϕ. On the other hand, the metabolism dose not end until the substrate was depleted. Then one can assume that it decreases exponentially with the time. Therefore, the metabolic rate can be established as follows:

$$Q_m(r,t,T)=Q_{m0}\cdot\phi^{[T(r,t)-37]/10}\cdot\exp(-t/\tau_0) \qquad (8)$$

where, Q_{m0} is the reference metabolic rate at $37\,^{\circ}C$, τ_0 is reference time at $37\,^{\circ}C$ and is estimated as 300 seconds. According to references [1], [2] ,[5], [6], ϕ is set as 3.0.

During the circulatory arrest, the transient oxygen behavior is governed by the reaction-diffusion equation:

$$\frac{\partial C_t}{\partial t}=D_t(T)\cdot\frac{1}{r}\frac{\partial^2(C_t r)}{\partial r^2}-M(C_t,T) \qquad (9)$$

with the boundary condition defined as $\partial C_t/\partial r=0$, $r=R_0$ and $\partial C_t/\partial r=0$, $r=0$ .The temperature dependent oxygen diffusion coefficient D_t is obtained from [7] as:

$$D_t(T)=a\cdot\exp\left[b\cdot T(r,t)\right] \qquad (10)$$

where $a=3.95\times10^{-10}\,\mathrm{m^2/s}$ is a constant, $b=4.6\%/^{\circ}\mathrm{C}$ is the temperature coefficient for diffusion.

Commonly the oxygen consumption can be treated as following the first-order kinetics, i.e., $M=\beta C_t$ [8]. Taking account of the effect of the temperature, we also assume that oxygen consumption varies with the local brain temperature. Subjected to these assumptions, the oxygen consumption rate is thereby expressed as:

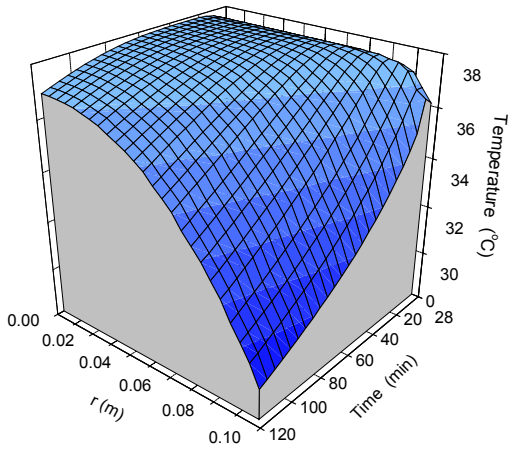
$$M(C_t,T)=\beta C_t\cdot\eta^{[T(r,t)-37]/10} \qquad (11)$$

where, $\beta=4.7\times10^{-3}\,\mathrm{s^{-1}}$ is a constant, and η is temperature coefficient and set as 2.5 [1].

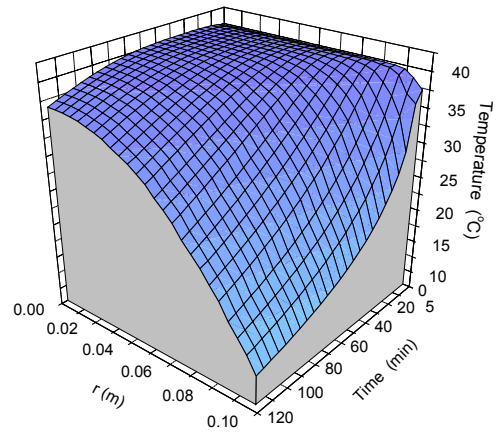
For the calculations, typical values for the thermal parameters were applied as given in [9]: $\rho=1.05\times10^3\,\mathrm{kg/m^3}$, $C_b\approx C=4200\,\mathrm{J/kg\cdot^{\circ}C}$, $K=0.5\,\mathrm{W/m\cdot^{\circ}C}$, $Q_{m0}=10000\,\mathrm{W/m^3}$. And $R_0=10\,\mathrm{cm}$ is used.

Ⅲ. RESULTS AND DISCUSSINS

Through numerical method, we calculate and analyze the transient brain temperature distribution and the oxygen concentration during circulatory arrest. Under normal condition (circulatory arrest doesn't occur), it can be regarded that the brain temperature is close to $37.24\,^{\circ}\mathrm{C}$, which is in agreement with the physiological data. Fig.1 (a) shows the brain temperature distribution during circulatory arrest with heat convection coefficient $h_f=10^{\circ}\mathrm{C}$ and surrounding air temperature $T_f=20^{\circ}\mathrm{C}$. Clearly, the temperature near the brain core ($r=0.01\mathrm{m}$) increases slightly at the beginning, which is mainly resulted from an unbalance between the high metabolic heat generation and the zero blood perfusion cooling. The temperature increase in the brain core at the beginning has also been reported by Xu et al. [5]. The brain core temperature decreases much more slowly than that at the brain surface. Even after a long period of time (say about 120 minutes), it still remains at about $36.15\,^{\circ}\mathrm{C}$.



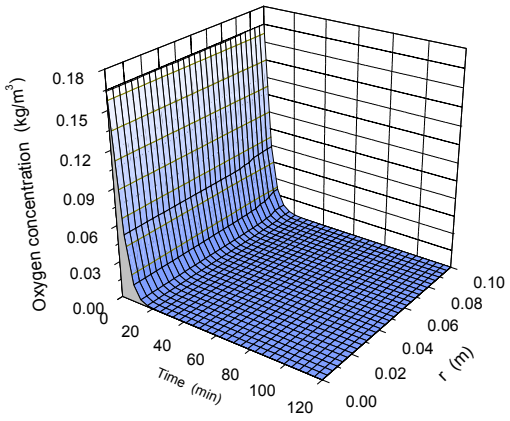
(a) surface air cooling: $h_f=10^{\circ}\mathrm{C}$, $T_f=20^{\circ}\mathrm{C}$



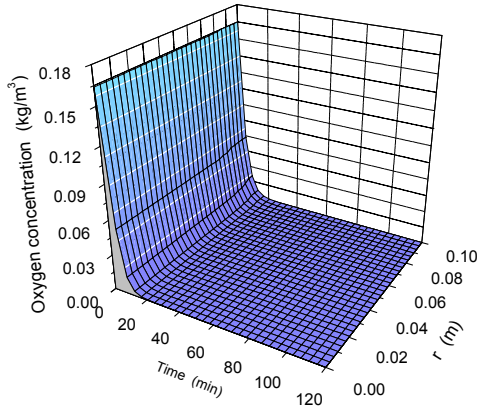
(b) surface ice-water cooling: $h_f=30^{\circ}\mathrm{C}$, $T_f=0^{\circ}\mathrm{C}$

Fig.1. Temperature distribution during circulatory arrest

To analyze the effect of hypothermia on the cerebral oxygen consumption rate, we use two approaches, the surface cooling (water flowing around the brain surface) and the volumetric cooling (inserting cooling probe into the deep brain or ventilating the cooling medium through the mouth and nose), to examine the effect of different cooling on the temperature development and the oxygen consumption.



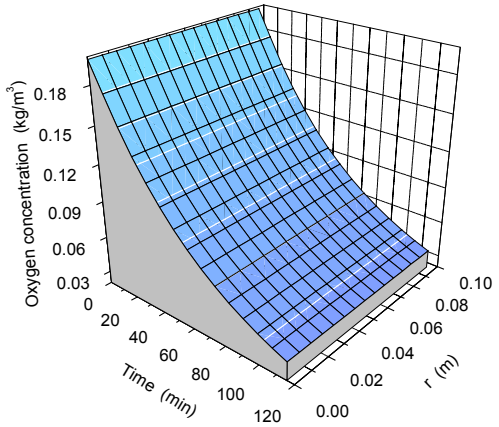
(a) surface air cooling: $h_f = 10^oC$, $T_f = 20^oC$



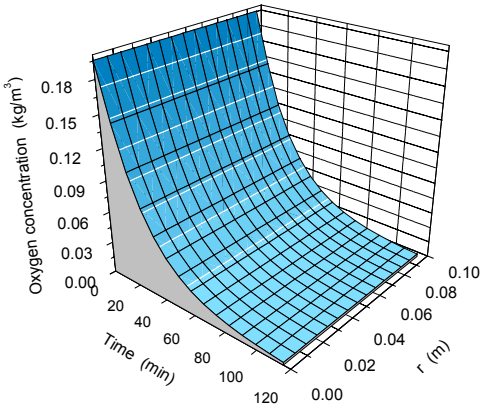
(b) surface ice-water cooling $h_f = 30^oC$, $T_f = 0^oC$

Fig. 2. The oxygen concentration distribution during circulatory arrest

Fig.1 (b) depicts the brain temperature distribution under convective cooling, $h_f = 30^oC$ and $T_f = 0^oC$. The temperature near the brain core ($r = 0.01$m) still increases slightly from 37.24 °C to the maximum 37.73 °C in about 26 minutes, then decreases slowly. The temperature on the brain surface can be significantly reduced by the convective ice-water cooling, but the effect of this cooling on the deep brain is not evident since it takes 82 minutes for the brain core temperature to change from 37.29 °C to 36.5 °C. These results are consistent with the previous clinical data. Surface cooling of head and irrigation of the nasopharynx with ice water lowered deep brain temperature from 37 °C to 34 °C only after 30-60 minutes [5]. Mellergard's [10] and Olsen et al's [11] studies also demonstrated that isolated head cooling, whether with frozen liquid or a cooling helmet, had a very limited effect on lowering the brain temperature. As shown in Fig.2, the oxygen consumption rate differs little between the two cases of $h_f = 10^oC$, $T_f = 20^oC$ and $h_f = 30^oC$, $T_f = 0^oC$. Overall, for surface cooling, the stored oxygen amount decreases sharply. It is almost completely depleted within less than 20 minutes. At this time, the oxygen concentration is three orders of magnitude lower than the initial oxygen concentration. From (10) and (11), it is seen that if the temperature of the brain can not be quickly reduced, both the oxygen diffusion coefficient $D_t(T)$ and the oxygen consumption rate $M(C_t, T)$ will keep at a higher value due to the weak cooling effect. Furthermore, the stored oxygen amount is depleted so quickly that it can not meet the basal metabolic requirement, which may cause the brain injury. Therefore, the surface cooling is in fact not very useful in reducing the oxygen consumption and thus preventing patients from the brain injure.



(a)



(b)

Fig. 3. The oxygen concentration distribution during circulatory arrest using volumetric cooling and the uniform brain temperatures are assumed as: (a) $T = 5^oC$ (b) $T = 15^oC$

In order to improve the brain hypothermia resuscitation and prolong the patient's survival time, an alternative cooling approach – the volumetric cooling is explored. In this way, a significant temperature decrease in the brain core can be realized by ventilating cold water to patient's circulatory system or directly inserting the cooling probe into the deep brain. The oxygen concentration distribution is depicted in Fig.3 on assuming that all the brain

temperature positions are fixed at a uniformly lowered temperature. Compared with the case of surface cooling, the oxygen concentration decreases much more slowly. When the uniform brain temperature alters from 15 °C to 5 °C , the average oxygen concentration decreases by 46% and 15% after about 20 minutes, respectively. Fig.4 clearly shows that at the region near the brain core ($r = 0.01\text{m}$) and under uniform volumetric brain temperature $T = 5^{o}\text{C}$, the oxygen concentration is still at about 0.0021 kg/m^3 at 20 minutes. Further calculations demonstrate that the oxygen consumption rate at this case is several orders of magnitude lower than that at the case of surface cooling. Therefore, it is likely that the temperature decrease in the whole brain ensures the oxygen demand sufficient to permit tolerance for a long period of absent oxygen delivery. In recent studies, Xu et al [6] pointed out that the circulatory cooling may be essential for a rapid brain cooling required for cerebral protection. Mariak et al's [12] experimental data demonstrated that heat loss from the upper respiratory tract can directly affect the intracranial temperature in human. But this method is not practically used, which is the issue to be solved.

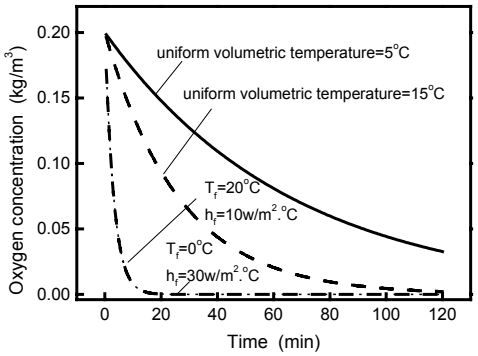


Fig.4. The effect of two cooling approaches on oxygen concentration in the inner brain region ($r = 0.01\text{m}$)

There are several assumptions and limitations in this study must be pointed out. First, it is assumed that blood perfusion immediately reduces to zero following the onset of circulatory arrests, which is the extreme case in the present simulation. However, calculations show that there is a negligible oxygen concentration difference between the case of zero perfusion and that of keeping perfusion unchanged for short time. In this model, it is simply assumed that the thermal properties are uniform, independent of space and temperature. In fact, the heat generation is a space dependent value. A spherical geometry is the simplest one that describes the one-dimension temperature distribution from interior of the brain to the skull. Therefore, we and other researchers [5] use this symmetrical geometry model. During circulatory arrest, the oxygen consumption rate is proposed to take the new form as (11). According to previous experimental study [1], the temperature coefficient considerably varies with the temperature. It falls in 2.0-3.0 at temperatures between 37 °C -28 °C . However, when temperature is less than 28 °C , the reported value is approximately two times of that at the higher temperature. In this paper, the temperature coefficient was treated as constant and equal to 3.0. However, although the oxygen consumption rate was perhaps overestimated at lower temperature, the above consideration does not change the conclusions substantially.

Ⅳ. CONCLUSION

Thermal factor is one of most important factors responsible for the oxygen delivery deficit. Results in this paper demonstrated that the surface cooling may provide some advantage by cooling the brain cortex peripherally. But its effect to depress the metabolic oxygen is very limited. In contrast, the volumetric cooling has the potential to substantially depress the oxygen metabolism, which points out the new way to develop high efficient cooling system. Further experiments and clinical practices will be performed in the near future to test our theoretical predictions.

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